FEATURED ACTIVITIES of DERT
May 2004

MEETINGS

Obesity: Developmental Origins and Environmental Influences
2004 Spring Symposium, Duke University Integrated Toxicology Program
National Institute of Environmental Health Sciences, NIH, DHHS
Friday, February 20, 2004
Duke University, Searle Center

Organizers: Edward D. Levin, Duke University and Jerry Heindel, COSPB

Background
Overweight and Obesity have reached epidemic proportions. This symposium focused on an underdeveloped aspect of the etiology of obesity that relates directly to the mission of NIEHS: the role of exposure to environmental chemicals *in utero* or neonatally in the development of obesity. In a recent review, Baille-Hamilton presented data on the role of chemical toxins in the etiology of obesity and showed the current epidemic coincides with the marked increase in chemical use in the environment. It is also apparent obesity is more prevalent in rural areas and inner cities where inhabitants are more exposed to environmental chemicals.

The first talk focused on epidemiological studies that have demonstrated a direct relationship between birth weight and BMI reached later in life. Fetal under-nutrition in mid to late gestation may particularly lead to obesity and the related metabolic changes. Similarly higher than average birth weight leads to increased BMI later in life. In addition, gestational diabetes leads to offspring that weigh more and are at increased risk of obesity later in life.

The increase of adipose tissue mass that accompanies obesity is due both to an increase in adipocyte number and size. Both processes can be mimicked *in vitro* using established stem and preadipocyte lines in culture. Using an immortalized multipotent stem cell line, C3H-10T1/2, researchers have shown that exposure to bone morphogenetic protein 4 leads to commitment to adipocytes. These preadipocytes can then be clonally expanded into adipocytes via treatment with cAMP, glucocorticoid and IGF-1.

Data on the role of estrogen and phytoestrogens in adipose tissue development and number show that estrogen in the adult is antilopolytic. Male and female estrogen receptor knockout mice have a 170% increase in adipocyte number. While the mechanism by which estrogen may inhibit increase in adipocyte number is unclear, recent data suggests a role for p27 and p21. A crucial question that remains unresolved is whether exposure of developing animals and humans to environmental estrogens such as phytoestrogens including genestein could alter adipocyte development and/or adult adipocyte number. Since so many human infants are fed soy based formula this is a question that has serious public health implications and needs investigation.

Fetal exposure to very low doses of the estrogenic chemical bisphenol A, which is the monomer used to make polycarbonate plastic, results in increased postnatal growth. As the amount of estrogenic contaminants in casein based animal feed increased, the amount of body fat decreased in mice indicating that particular attention must be paid to the contents of feed when one is studying obesity. In a related finding casein-based diets with no estrogenic activity resulted in higher estrogen levels in the pups, which were were born heavier. These animals grow up to be fatter and heavier and appear to develop the metabolic syndrome of obesity, diabetes, and insulin resistance. Some of these animals have been shown to have high leptin levels indicating leptin resistance. These data suggest that *in utero* estrogens may be adipogenic, an effect opposite that found in adults.

In utero and neonatal exposure to diethylstilbestrol (DES), a synthetic estrogen, affected body weight. High doses neonatally caused a decrease in body weight in the adult while low doses of DES (.001mg/kg/d) caused a significant increase in body weight in mice. The body weight of DES treated pups was normal after treatment but increased gradually over the lifetime of the mice. In adulthood the weight of the mice was 3-4 times normal. Neonatal exposure to genestein, a phytoestrogen, caused a significant increase in body weight by three months of age.

Environmental chemicals may also affect obesity via the sympathetic nervous system. Central and sympathetic norepinephrine systems are critically involved in the control of adipose tissue metabolism and appetite. A low dose of nicotine administered to mice during gestation results in significant weight gain after birth. This effect may be mediated via blunting of sympathetic and central norepinephrine systems which normally act to increase lipolysis and reduce appetite.

Outcomes
After the day long meeting the presenters participated in a brainstorming session to analyse the state of the art and suggest research needs. Several points were raised:

- There are sufficient data to warrant further study of the role of *in utero* exposures to environmental chemicals in the etiology of obesity. Focus should be on environmental chemicals with estrogenic activity as well as agents that can alter central nervous system function so that control of appetite in addition to direct effects on adipose tissue development and differentiation would be assessed.

- There should be a focus on developing the data on the safety of *in utero* and neonatal exposures to phytoestrogens, via soy formula, on later onset of obesity.

- Diet is critical when studying *in utero* effects of environmental chemicals on obesity. Thus synthetic diets should be encouraged. Studies on the interaction of diet and environmental chemical exposures should also be encouraged.

- Mechanistically, NIEHS should encourage studies of altered gene expression during development after exposure to environmental chemicals and to assess epigenetic changes that could result in altered tissue function later in life.

- NIEHS should be encouraged to stimulate this field via specific initiatives. (Note: NIEHS has added obesity to the latest iteration of the Fetal Basis Program Announcement as a result of this recommendation)

- NIEHS should be encouraged to work with NIDDK to develop a larger more comprehensive meeting on obesity with a focus on the fetal basis of obesity for 2005.

A complete video of the symposium is available at
http://www.niehs.nih.gov/multimedia/gt/dert/obesity/agenda.htm

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Workshop on Structural Determination of Environmentally Responsive Gene Products
April 12 – 13, 2004
Snowbird, Salt Lake City, Utah

Organizers: Les Reinlib, PhD (SPHB), David Balshaw, PhD (CRIS), Pat Mastin, PhD (COSPB)

Objectives
The objective of this workshop was to bring together experts in genomics, structural biology, pharmacology, and related cutting-edge technologies (computer modeling, X-ray crystallography, NMR, mass spectroscopy) to identify the optimal routes to solving 3-dimensional structures of environmental

response gene (ERG) products and protein pathways. This information is expected to stimulate new avenues of research on understanding how gene variations underlie altered protein structures and functions. Ultimately, these studies are expected to lead to insights into susceptibility to environmental diseases and to improved ligand and drug design for research, patient therapy, and screening. The workshop recommendations will be published as a guide to the NIEHS in program development and to the research community.

Recommendations
The Workshop Participants recommended support of integrated projects to exploit the talents of mathematicians, computer scientists, and biologists. Outstanding workers in these fields approach their subject matter from disparate viewpoints and appear to speak in different languages. The participants strongly recommended training of young investigators as an important component of new initiatives. Trainees with backgrounds in biochemistry, molecular biology, physiology, etc. would gain valuable skills in mathematics and computer science courses that could be well applied to the issues central to environmental health sciences.

Highest Priorities
- Support studies of structure, analysis, control, and design of conformational and functional states at molecular resolution for environmentally-responsive molecules and complexes.
- Encourage integrated experimental and computational approaches
- Promote understanding of dynamics, kinetics, and ligand responses
- Investigate the mechanisms and steps in post-translational modifications, protein partnering, impact of genetic polymorphisms on structure/function, and ligand interactions

Mid-level Priorities
- Improve the production of protein samples and macromolecular assemblies (e.g. environmentally responsive membrane proteins)
- Develop optimal processes for design, production, and assembly of macromolecular complexes

Lower Priorities
- Encourage studies on protein-protein (macromolecules) interactions
- Examine assemblies and pathways rather than individual proteins

21st International Neurotoxicology Conference: Infant and Child Neurotoxicity Studies
February 10-14, 2004
Honolulu, Hawaii

Background
A number of NIEHS staff attended and participated in this conference organized by Dr. Joan Cranmer, Professor of Pediatrics, University of Arkansas, and member of the National Environmental Health Sciences Advisory Council. A significant highlight was that for the first time all the major longitudinal children's studies addressing the important persistent pollutants were presented together. This provided a unique opportunity to make significant advances in our understanding of the subtle and latent effects that these chemicals – alone or in combination – may be posing to children. The overall program focused on mechanisms and consequences of developmental neurotoxicity in children and experimental animals from exposure to persistent pollutants (e.g., pesticides, metals and industrial chemicals) during development (i.e., embryonic, fetal, neonatal, infant, child and/or adolescent). The conference debated the most recent basic and clinical research advances, risk-assessment approaches, pediatric cognitive/neurobehavioral tests and batteries, problems and interpretation of issues unique to epidemiological studies of children, ethical/legal issues and related information concerning children's health and exposure to persistent pollutants. Products of the conference will be peer-reviewed and rapidly published papers in *Neurotoxicology.*

Conference Objectives

The Conference met each of its specific aims:

- To provide an internationally recognized, interdisciplinary scientific forum for presentation of the major longitudinal children's studies investigating the low-level and long-term effects of methylmercury, PCBs, lead, heptachlor, other pesticides and mixtures.

- To conduct an Open Public Forum/Town Meeting for clinical and basic scientists, clinicians and the citizens of Hawaii who were involved in the 20-year heptachlor studies. To facilitate communication between the researchers and the parents and children from Hawaii who were exposed to heptachlor in pineapple chop and contamination of the milk supply and to discuss the implications of study results.

- To convene scientists from different scientific domains to exchange data and theories regarding the etiology, mechanisms, diagnosis, treatment and prevention of environmentally-induced diseases and disorders of the nervous system in the fetus, infant, child, adolescent, and adult (latent effects). To provide ample time and an environment for informal scientific exchange to promote collaborations and networking worldwide.

- To encourage and recognize student research endeavors by offering pre-doctoral and post-doctoral awards (cash and plaques) and travel scholarships and to provide mentoring and networking opportunities

The internationalization of children's environmental health was a reoccurring theme throughout the Conference. Dr. Henry Falk, Director, National Center for Environmental Health/CDC and Assistant Administrator, ATSDR, gave a Keynote Address focusing on the international perspective to children's environmental health. Dr. Suk, CRIS, and Dr. J. Satayavivad, Chulabhorn Research Institute, Bangkok, Thailand, organized and co-chaired a session on emerging issues in children's environmental health from an international perspective.

A significant part of the Conference was dedicated to the NIEHS/EPA Children's Centers. Dr. Collman, SPHB, and Dr. Chris Saint, U.S. EPA organized and co-chaired a series of sessions focusing on the critical results coming from these research and prevention programs. Dr. Collman provided an overview of this Center's program. Dr. Dick Jackson, Senior Advisor to the CDC Director gave a Keynote Address on children's health in relationship to obesity, urban and suburban sprawl and environmental health issues.

The final Keynote Address was given by Dr. Duane Alexander, Director, National Institute of Child Health and Human Development, NIH, whose presentation focused on the National Children's Study and its importance in reducing the risk of childhood diseases as well as future risk of chronic diseases in childhood.

The Conference was sponsored by the NIEHS, the National Center for Environmental Health/CDC, and the National Center for Environmental Assessment/U.S. EPA; co-sponsors included the National Institute of Child Health and Human Development, the National Institute on Aging, and the NIEHS Superfund Basic Research Program; contributors included ATSDR, Arkansas Children's Hospital, Chulabhorn Research Institute, and Society of Toxicology.

Following the Conference NIEHS sponsored a Town Meeting entitled "Environmental Health Concerns in Hawaii" to stimulate effective dialogue between the citizens of Hawaii and local, state and national environmental public health scientists, practitioners and policy makers. Dr. Ken Olden, Director, NIEHS, gave the Keynote Address entitled "Bringing the Benefits of Environmental Health Research to the Public." Dr. Bruce Anderson moderated sessions dealing with environmental health concerns of the Hawaii population. Panels of experts presented on the respiratory health effects of volcanic gases, human health and the ocean environment, the long-term effects of the Hawaii heptachlor contamination, and autism and the environment. General discussion of environmental concerns followed.

Outcomes
Papers from this meeting will be published in a peer-reviewed special issue of *Neurotoxicology* entitled "Infant and Child Neurotoxicity Studies."

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NIEHS Nanotechnologies Workshop: Technologies for Improved Risk Stratification and Disease Prevention
March 11-12, 2004
Rodbell Auditorium, NIEHS

Drs. Balshaw and Suk, CRIS, organized a panel of experts charged with assessing the current state of the science in nanotechnologies and formulating a list of specific recommendations for applying nano- and micro- scale devices in the environmental health sciences. The ultimate goal of the initiative is to develop tools to improve public health through improvements in risk assessment, individual risk stratification and the prevention of environmentally induced disease. The workshop was divided into three separate topics: Sensors and BioMEMS (microelectromechanical systems) for risk assessment, tools for mechanistic and functional investigations, and nanoscale devices for environmental remediation. The group agreed that it is important to be broad in defining nanotechnology, focusing on the benefits gained in decreasing scale, both in reagent utilization and in the emergent physical and chemical properties rather than focusing on a particular range of dimensions. This brief report summarizes the highlights of the meeting with a full report being prepared for publication.

Meeting Highlights
Decreasing the experimental scale has a number of advantages, both in terms of practical benefits and the emergence of novel chemical and physical properties. The practical benefits include decreased requirements for expensive reagents including probes and enzymes and an increased ability to automate and multiplex experiments. There are also a number of emergent chemical and physical properties that emerge at the nanoscale, most notably in the optical properties of nanoengineered fluorophores, which have extremely long fluorescence lifetimes, high quantum yields and often, as in the case of quantum dots, tunable emission and excitation profiles.

Environmental monitoring: One of the major barriers in the environmental health sciences is the relative lack of monitoring tools that are both highly specific to known agents and that have sufficient throughput to allow comprehensive 'real time' assessment. It is currently possible to develop micro- and nano-scale arrays, primarily based on affinity reagents that can detect specific sets of harmful agents in the environment. Provided adequate informatics support; this monitoring can be done in 'real time' and remotely accessed. These micro- and nano-scale environmental monitoring systems can also be extended to the individual level, detecting individual exposures and tissue distributions of toxins and environmental agents, and can possibly be coupled with catalytic or chelating activity. The resulting 'smart' sensors could represent an NIEHS specific platform technology, the development and use of which will enhance our ability to link relevant exposures to populations, and thereby, aid epidemiologic investigations and improve public health.

Relating physiological responses to environmental perturbations: Perhaps the major challenge facing the environmental health sciences as a whole is the ability to relate a given internalized dose of toxin to a phenotypic response. Understanding this relationship will require the development of tools for monitoring the signaling mechanisms involved in the pathological response with quantitative data with high temporal and spatial resolution. A number of nanoscale tools are emerging to accomplish this including primarily fluorescence based probes targeted towards small molecule second messengers and quantum dots which can be used to tag specific proteins. It is also possible that these tools can be engineered not only to detect physiological responses to exposures but also to intervene and reduce the development of disease or to treat existing disease. Current examples of nanoscale therapeutics include nanoshells, gold coated mica beads that target tumor tissues.

Nanoscale tools for environmental remediation: Within the realm of tools for environmental remediation, no single factor is more important than surface area. Given that volume increases with the cube of radius while surface area increases with radius squared; the ratio of surface area to volume, therefore, increases dramatically at the nanoscale. One specific example given in the workshop was for Self Assembled Monolayers on Mesoporous Supports (SAMMS) for which a 2 tablespoon volume has the surface area of a football field. There are essentially two applications of nanoscale tools for remediation: chelating agents and catalytic agents. Chelating agents, which are particularly useful for metals and radioactive materials, merely bind the hazardous agents with very high affinity effectively immobilizing and concentrating the agent for long-term storage. In some cases these can be landfill approved entities greatly reducing the cost of storage. Catalytic agents on the other hand, convert the hazardous agent into a non-toxic form either through reduction or oxidation or through chemical changes such as dehalogenation of organics.

The Long Range Recommendation: The participants were unanimous in embracing an idea that the NIEHS lead the way in developing a single, small scale platform technology that would combine aspects of each of the above recommendations to prophylactically detect an individual exposure, eliminate the toxin from the system and intervene to reverse any harmful effects that may have been initiated. This may appear to be science fiction from the imaginations of Dan Brown, Michael Crighton or Isaac Assimov; however, the technology to develop such probes is readily achievable within the not too distant future.

DERT IN THE NEWS

Centers for Oceans and Human Health

"The National Science Foundation (NSF) and the National Institute of Environmental Health Sciences (NIEHS), one of the National Institutes of Health, have announced funding for four joint Centers for Oceans and Human Health (COHH). The centers will be located at the University of Washington, the University of Hawaii, the Woods Hole Oceanographic Institution in Massachusetts, and the University of Miami.

The centers will bring together experts in biomedical and oceanographic sciences for the first time to study the effects of harmful algal blooms, marine pathogens, and the oceans' vast potential for drug discovery. The combined expertise of the participants will accelerate the pace of scientific discovery, ranging from the development of new sensors for early warning systems to enhanced progress in finding novel compounds with pharmaceutical potential."

See http://www.niehs.nih.gov/oc/news/ocean.htm for the full press release.

Study Shows Effects of Prenatal Exposure to Second-Hand Smoke Greater for Socioeconomically Disadvantaged Children

Researchers at the Columbia Center for Children's Environmental Health report in the March 2004 issue of the journal *Neurotoxicology and Teratology* that "the effects of prenatal exposure to second-hand smoke on mental development are exacerbated in children who experience socioeconomic hardships, such as substandard housing and inadequate food and clothing, during the first two years of life.

While the study results indicate that prenatal exposure to second-hand smoke can be harmful to the unborn child regardless of socioeconomic conditions, the data also suggest that lower-income children may be less able to compensate for these effects over the next few years of life."

See http://www.niehs.nih.gov/oc/news/shsmoke.htm for the full press release.

First Human Study to Show Benefits to Newborns from Federal Ban on Home Use of Two Insecticides
A federal ban on two insecticides, chlorpyrifos and diazinon, has resulted in a significant reduction in their impact on newborns' birth weight and length, report researchers at the Columbia University Center for Children's Environmental Health.

See http://www.niehs.nih.gov/oc/news/insect.htm for the complete press release.

The Worker Education and Training Program (WETP) supports the training and education of workers engaged in activities related to hazardous materials and waste generation, removal, containment, transportation and emergency response. Recently two articles highlighted how some of these funds are being used. In Boston, unemployed and underemployed persons are training to become environmental cleanup technicians. For the full article, which appeared in the Boston Globe April 23, see:
http://www.boston.com/news/globe/editorial_opinion/editorials/articles/2004/04/23/job_training_that_works/

On April 8, the Times Ledger reported on a three-day hazardous materials training course taken by Jamaica Hospital Medical Center staff. The 30-person class, comprised of emergency room, housekeeping, building maintenance and other staff, was designed to familiarize staff with the process and equipment used to decontaminate patients who might pose a risk to other patients inside the hospital. For the complete story see:
http://www.timesledger.com/site/news.cfm?newsid=11267920&BRD=1079&PAG=461&dept_id=170338&rfi=8

New Research Outlines Public Health Consequences of World Trade Center Disaster
Results from longitudinal studies of firefighters, rescue workers and other personnel who responded to the collapse of the World Trade Center show profound exposure-related adverse effects on the respiratory system.

See: http://www.nih.gov/news/pr/may2004/niehs-03.htm for the complete press release.

DERT PAPERS OF NOTE

Oxidase Enzyme is the Target for Arsenic-Induced Reactive Oxygen Species Production in Leukemia Cells
Michael A. Trush, Ph.D.
The Johns Hopkins University School of Medicine
NIEHS Grants R01ES03760 and P30ES03819

Background: Arsenic is a naturally occurring metal-like element found widely and in varied forms in the environment. Inorganic forms of arsenic are considered the most toxic and are found in drinking water, soils, and geologic formations. Humans can be exposed to arsenic in a variety of ways; however drinking contaminated water and industrial exposures are the most common. Arsenic is acutely toxic to humans at doses that generally occur through accidental or intentional poisonings. Arsenic is a known carcinogen to humans; skin cancer is the most common form of malignancy; however, other cancers of the lung, bladder, liver, kidney, and prostate can also occur following arsenic exposure. Interestingly, arsenic has been used for centuries in traditional folk remedies and today it is a component of cancer chemotherapeutic agents. Recently, much attention has been paid to the dramatic clinical efficacy of arsenic against acute promyelocytic leukemia.

Advance: Arsenic is known to induce the formation of reactive oxygen species (ROS); however, the mechanism has previously been undefined. Using gene expression profiling, interference RNA, and genetically engineered cells, these investigators determined that an enzyme required for the normal antibacterial function of white blood cells known as NADPH oxidase is the main target for arsenic-induced ROS production. NADPH oxidase can also be stimulated by a compound known as phorbol myristate.

The investigators went on to show that arsenic and a clinically used analog of phorbol myristate, bryostatin 1, synergistically act to enhance ROS production.

Implications: These investigators have shown that very low levels of arsenic and bryostatin 1 can effectively kill leukemic cells. The findings identify the arsenic target of ROS production and provide a new concept for an anticancer treatment that may have decreased adverse side effects. These findings may also provide clues to the carcinogenic potential of arsenic.

Citation: Chou WC, Kie C, Kenedy AA, Jones RJ, Trush MA, Dang CV. Role of NADPH oxidase in arsenic-induced reactive oxygen species formation and cytotoxicity in myeloid leukemia cells. Proc Natl Acad Sci USA. 2004 Mar 30; 101(13):4578-83.

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Production of a Vaccine for Prostate Cancer Immunotherapy
Maarten C. Bosland, DV.Sc., Ph.D., New York University Medical Center
NIEHS Grant P30ES00260.

Background: The prostate gland is dependent on testosterone produced in the testes for growth and function. Therefore, reducing the production of testosterone is a targeted therapy in prostate cancer patients. Testosterone is produced in response to a hormone from the pituitary gland called luteinizing hormone. Luteinizing hormone is released from the pituitary in response to luteinizing hormone-releasing hormone (LHRH), which is produced in the hypothalamus. Each step in this pathway provides an opportunity to block the production of testosterone to slow the growth of prostate tumors. These investigators using resources at the NIEHS-funded Center at the New York University Medical Center describe a vaccine against LHRH.

Advance: The vaccine was created using sophisticated immunological techniques and tested in rodents, dogs, and baboons. The vaccine produced anti-LHRH antibodies in all three species. This vaccine differs from others in use in that it targets LHRH itself and not a carrier protein. The vaccine, in a clinically applicable formulation, controlled the growth of androgen-responsive prostate tumor cells in rats.

Implications: The results of these studies demonstrate an efficient, responsive, and long-lasting decrease in androgen production in three diverse species, one of which is a non-human primate. Further studies are needed to determine if the vaccine is safe and effective at blocking testosterone production and prostate tumor growth in humans. If results from these studies are favorable, the vaccine could be an improved, less invasive method for treating prostate cancer.

Citation: Finstad CL, Wang CY, Kowalski J, Zhang M, Li ML, Li XM, Xia WG, Bosland MC, Murphy KK, Walfield AM, Koff WC, Zamb TJ. Synthetic luteinizing hormone releasing hormone (LHRH) vaccine for effective androgen deprivation and its implication to prostate cancer immunotherapy. Vaccine. 2004 Mar 12; 22(9-10):1300-13.

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A Mutation in the Hepatitis B Virus Predicts Liver Cancer Development
Alvaro Munoz, Ph.D., Thomas Kensler, Ph.D., and John Groopman, Ph.D.
The Johns Hopkins University Bloomberg School of Public Health
P01ES06052 and P30ES03819

Background: Liver cancer is the fifth most prevalent form of cancer worldwide causing over 427,000 deaths in 1990. Exposure to the hepatitis B virus is a major risk factor for the development of liver cancer. Previous work by this investigator has shown that hepatitis B exposure causes a 7-fold risk. Exposure to aflatoxin, a mold commonly found in peanuts and grains, increases the risk of liver cancer by 3.5 times. These two agents combined cause a remarkable 60-fold increase in risk of liver cancer. This is an

especially troubling public health problem in China where hepatitis B and aflatoxic exposure are both very high.

Advance: The current study by this NIEHS-supported investigator examines a particular mutation in the hepatitis B virus. Studies were conducted of the prevalence of the mutation in plasma and tumors of from patients living in Qidong, People's Republic of China. Initial studies determined that about three-fourths of the tumors from the patients contained the mutation. The investigators went on to determine that plasma samples contained the virus mutation about half the time before cancer had appeared.

Implications: These findings suggest that detection of the mutated hepatitis B virus is an early warning sign of subsequent liver cancer development. Early detection, even before liver cancer can be detected, is very important in prevention and intervention trials and may lead to better treatment outcomes.

Citation: Kuang SY, Jackson PE, Wang JB, Lu PX, Munoz A, Qian GS, Kensler TW, and Groopman JD. Specific mutations of hepatitis B virus in plasma predict liver cancer development. Proc Nat Acad Sci USA. 2004 Mar 9; 101(10):3575-80.

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Drug Used to Arrest Preterm Labor Sensitizes the Brain to Neurotoxins
Theodore A. Slotkin, Ph.D., Duke University Medical Center
NIEHS Grants T32ES07031, P42ES10356, and R01ES10387

Background: There is a growing body of evidence that suggests that exposure to environmental agents *in utero* or very early after birth can have life-long effects. This phenomenon is referred to as the fetal basis of adult disease. It is of growing concern to NIEHS and environmental health scientists worldwide. Hypertension, diabetes, asthma, and cardiovascular diseases are but a few of the illnesses that have been suggested as possible effects from these early-life exposures. This investigator examined the combined exposures of terbutaline, a drug used to arrest preterm labor, and subsequent exposure to the organophosphate pesticide chlorpyrifos on several indices of brain cell growth and function.

Advance: Young rats were given terbutaline on days 2-5 after birth, followed by chlorpyrifos on days 11-14. Neither treatment affected growth or viability of the young rats; however, both elicited alterations in brain cell differentiation and cholinergic innervation at day 15 persisting into adulthood (day 60). Biomarkers of brain cell number, cell size, and neuritic projections were affected by either agent alone; however the combined exposure produced more severe effects.

Implications: These findings suggest that terbutaline is a developmental neurotoxicant much like chlorpyrifos. The authors conclude that the use of terbutaline to prevent preterm labor may be creating a subpopulation that is more sensitive to the adverse neural effects of organophosphate pesticides. Further studies are needed to repeat these findings, but if the results are confirmed, use of these compounds may need additional scrutiny.

Citation: Rhodes MC, Seidler FJ, Qiao D, Tate CA, Cousins MM, Slotkin TA. Does pharmacotherapy for preterm labor sensitize the developing brain to environmental neurotoxicants? Cellular and synaptic effects of sequential exposure to terbutaline and chlorpyrifos in neonatal rats. Toxicol Appl Pharmacol. 2004 Mar 1; 195(2):203-17.

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Economic Benefits of Air Pollution Reduction for Children
Elaine M. Faustman, Ph.D.
University of Washington
P01ES09601

Background: The health effects of air pollution have been reported in many research studies over the past 30 years. These effects include mortality, respiratory and cardiovascular diseases and hospitalizations, changes in lung function, asthma attacks, and days lost from school and work. The need for cost-benefit analyses of environmental regulations has become increasingly important in the U.S. to warrant the high costs. Children are significantly affected by air quality; however, previous environmental regulation has not focused effects seen exclusively in children. These researchers used a meta-analysis approach to determine the child-specific health impacts derived from the U.S. Clean Air Act.

Advance: The researchers determined, based on data from published studies, that reductions in the criteria air pollutants (particulate matter, ozone, carbon monoxide, sulfur dioxide, nitrogen dioxide, and lead) predicted to occur by 2010 in response to Clean Air Act regulations would have the following impacts: "200 fewer expected cases of postneonatal mortality; 10,000 fewer asthma hospitalizations . . . with estimated benefits ranging from $20 million to $46 million (1990 U.S.$); 40,000 fewer emergency department visits in children . . . with estimated benefits ranging from $1.3 to $5.8 million; 20 million school absences avoided . . . with estimated benefits of $0.7 to $1.8 billion; and 10,000 fewer infants of low birth weight, with estimated benefits of $230 million." Including the child-specific data "would be expected to add $1-2 billion to the $8 billion in health benefits currently estimated to result from decreased morbidity, and $600 million to the $100 billion estimated to result from decreased mortality."

Implications: The results of this study suggest that air pollution represents a significant health and economic burden to children in the U.S. The authors state that their estimates of health benefits are conservative and conclude that these estimates highlight the need for increased consideration of children's health effects in environmental regulation. They also point out that improved information for children's health effects and health economics are needed for more thorough environmental policy analyses.

Citation: Wong EY, Gohlke J, Griffith WC, Farrow S, Faustman EM. Assessing the health benefits of air pollution reductions for children. Environ Health Perspect. 2004 Feb; 112(2):226-32.

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Inhibition of Testosterone Production by the Environmental Estrogen Bisphenol A is Associated with Decreased Luteinizing Hormone Secretion and Decreased Steroidogenic Enzyme Gene Expression in Leydig Cells
Matthew P. Hardy, Ph.D.
Center for Biomedical Research, The Population Council
R01ES10233

Background: Synthetic estrogens have been implicated in a variety of endocrine related diseases such as hypospadias and testicular, prostate, and breast cancers. These compounds, also called xenoestrogens, are a diverse group of substances that mimic the action of the natural hormone, 17b-estradiol, in estrogen responsive tissues. Agents that cause adverse effects in target organs and tissues act by interfering with the actions of endogenous hormones and receptors. NIEHS-sponsored investigators at The Population Council have identified such effects from exposure to bisphenol A. Bisphenol A is a component of polycarbonate plastics and resins used in food packaging and dentistry.

Advance: These investigators exposed young laboratory rats to bisphenol A at low levels approximating that found in the environment. They found significant decreases in luteinizing hormone (which stimulates the production of testosterone in Leydig cells in the testis) and testosterone in serum samples. They also

noted a decrease in the gene expression level of pituitary luteinizing hormone receptor and an increase in pituitary estrogen receptor gene expression. *In vitro* experiments with cultured Leydig cells also showed reductions in testosterone production after exposure to bisphenol A. A final set of experiments in which pregnant and nursing rats were administered bisphenol A showed a marked decrease in testosterone in testicular interstitial fluid of their male offspring.

Implications: These studies indicate that the perinatal period is a sensitive window of exposure to bisphenol A. The authors conclude that suppression of steroid hormone synthesis may be responsible for testicular abnormalities associated with bisphenol A in laboratory studies. Although there is no evidence of adverse effects in humans who consume bisphenol A orally from plastic food packaging, this exposure and the extensive use of bisphenol A in consumer products warrants more investigation of this compound at low doses for the purposes of risk assessment.

Citation: Akingbemi BT, Sottas CM, Koulova AI, Klinefelter GR, and Hardy MP. Inhibition of Testicular Steroidogenesis by the Xenoestrogen Bisphenol A is Associated with Reduced Pituitary Luteinizing Hormone Secretion and Decreased Steroidogenic Enzyme Gene Expression in Rat Leydig Cells. Endocrinology 145:592-603, 2004.

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Risk of Salivary Tumors Following Gamma Radiation Exposure
Qingyi Wei, MD, Ph.D.
The University of Texas M.D. Anderson Cancer Center
R01ES11740

Background: Salivary glands have been shown in previous research to be highly sensitive to radiation exposure. Exposure to gamma radiation (ie. X-rays) is a known risk factor for both benign and malignant salivary gland tumors. However, the precise mechanism for this adverse effect has not been determined. The focus of this study was to determine whether radiation-induced chromosome breaks are a risk factor for benign and malignant tumors and whether there were any differences in risk between the two types of tumors.

Advance: The authors performed a pilot case-control study of 57 salivary gland cancer patients and 105 controls with no history of salivary gland cancer. Blood lymphocytes were collected and cultured from all research participants. The blood cells were exposed to a single dose of gamma radiation. Five-hours later, slides of the exposed cells were prepared so that counts of chromosome breaks could be determined. There were highly significant increases in the number of breaks/cell from the lymphocytes of the salivary cancer patients. The patients with malignant salivary gland tumors were 40 times more likely to have breaks/cell values higher than the median of the controls. Patients with benign tumors were less likely (4.7 times) to have elevated breaks/cell as compared to the controls.

Implications: Although this study was small and needs to be confirmed in larger studies, it does show that exposure to gamma radiation is a likely risk factor for malignant and benign salivary tumors. If larger studies do indeed confirm these results, this finding could have public health implications regarding the frequency of use of gamma radiation in the practice of dentistry.

Citation: Zheng R, Wang LE, Bondy ML, Wei Q, Sturgis EM. Gamma radiation sensitivity and risk of malignant and benign salivary gland tumors: a pilot case-control analysis. Cancer. 2004 Feb 1; 100(3):561-7.

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Expression of DNA Repair Genes is Sensitive Marker for Oxidative Stress
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Background: Oxidative damage to DNA is known to be one of the mechanisms leading to the development of cancer after exposure to environmental agents. Studies have shown that chemical carcinogens that increase the production of reactive oxygen species also induce the formation of oxidative DNA lesions. All aerobic organisms have evolved methods to repair this damage known as DNA adducts. Adducts have been used extensively as markers for environmental damage to DNA; however, in many studies oxidants fail to produce adducts. Thus, these researchers thought that expression of genes involved in DNA repair might be a more sensitive marker for exposure and effect.

Advance: To test the hypothesis, mice were given the chemical carcinogen and peroxisome proliferator WY-14,463. Peroxisomes are intracellular organelles that metabolize lipids and are found in high concentrations in liver cells. Peroxisome proliferators are compounds that stimulate a marked increase in the number and size of peroxisomes in liver tissue and are thought to contribute to carcinogenesis by generating reactive oxygen species that damage DNA. Treatment with WY-14,463 failed to produce differences in a number of conventional end points that are commonly used to assess oxidative DNA damage. However, there was a marked increase in the expression of genes responsible for a specific pathway of DNA repair that removes oxidative damage. Furthermore, this novel marker of oxidative DNA damage was used to elucidate how WY-14,463 causes production of oxidants that damage DNA.

Implications: The studies suggest that gene expression analyses can be used as sensitive markers for chemically-induced oxidative DNA damage. In this study, the gene expression changes for a DNA repair pathway specific for removal of oxidized lesions were seen at a dose that did not produce common markers of oxidative damage; therefore, these gene expression analyses could be a used as a more sensitive measure. Additional studies are needed to corroborate these results in other model systems where oxidative damage to DNA is thought to play a role in cancer but no firm experimental evidence is yet available.

Citation: Rusyn I, Asakura S, Pachkowski B, Bradford BU, Denissenko MF, Peters JM, Holland SM, Reddy JK, Cunningham ML, Swenberg JA. Expression of base excision DNA repair genes is a sensitive biomarker for in vivo detection of chemical-induced chronic oxidative stress: identification of the molecular source of radicals responsible for DNA damage by peroxisome proliferators. Cancer Res. 2004 Feb 1;64(3):1050-7.

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GRANTEE HONORS and AWARDS

Dr. Thomas Arcury, Professor, Wake Forest University School of Medicine, will receive the 2004 Outstanding Researcher Award by the National Rural Health Association at the association annual meeting in San Diego, CA, on May 26. This award is based largely on the projects improving the health of migrant and seasonal farm workers he has directed.

Dr. Gerald N. Wogan, Professor of Toxicology and Professor of Chemistry at the Massachusetts Institute of Technology, has been selected to receive the 2004 Distinguished Lifetime Toxicology Scholar Award for his substantial and seminal scientific contributions to the discipline of toxicology.

Dr. Melvin E. Andersen, CIIT Centers for Health Research, received the Arnold J. Lehman Award at the 2004 Annual Meeting of the Society of Toxicology. Dr. Anderson is widely recognized for contributions in strengthening the scientific basis of chemical risk assessment.

The Board of Publications of the Society of Toxicology announced the best paper published in Toxicological Sciences during the past year to be: Inhaled Environmental Combustion Particles Cause Myocardial Injury in the Wistar Kyoto Rat. Urmila Kodavanti, Carolyn Moyer, Allen Ledbetter, Mette Schladweiler, Daniel Costa, Russ Hauser, David Christiani and Abraham Nyska (ToxSci 71, 237-245, 2003). *Drs. Hauser and Christiani*, both of Harvard University, are NIEHS grantees.

Dr. Jay Gandolfi, Professor of Anesthesiology, Pharmacology, and Toxicology in the Department of Pharmacology & Toxicology at the College of Pharmacy of the University of Arizona was the recipient of the Society of Toxicology's Education Award.. Throughout his academic career he has maintained a strong focus on education, research, and collaborative programs.

The 2004 SOT/ACC Early Career in Neurotoxicology Award is presented to *Nikolay Filipov* of Mississippi State University. Dr. Filipov, an NIEHS grantee, was selected for his proposed research entitled Dopaminergic Toxicity of Chronic Exposure to the Herbicide Atrazine Interfaced with Short-Term Exposure to Maneb. Dr. Filopov plans to continue his research on susceptibility of the aged to environmental chemicals, an area very important for risk assessment.

This year's recipient of the AstraZeneca Traveling Lectureship Award is *Dr. Charlene McQueen*. Dr. McQueen, an NIEHS grantee, is a professor in the Department of Pharmacology and Toxicology, College of Pharmacy at the University of Arizona. Her research focus is currently on fundamental studies of the role of genetic variation in susceptibility to aromatic amine and hydrazine toxicity.

On April 20, 2004 the U.S. EPA recognized organizations and individuals in recognition of their efforts to protect and preserve the environment in 2003. Two of the honorees are affiliated with NIEHS-funded projects. *Ms. Liliana Guzman*, a junior at San Diego High School, "has become an asset to her community and to the local community group Environmental Health Coalition, by taking a leading role in educating, organizing and advocating for environmental health and justice in her community." *Dr. Henry Gong, Jr., M.D.*, is a practicing lung physician and past director of the USC Center for Children's Environmental Health. He integrates his clinical and research skills into educating others about the health effects of air pollution. "His extensive clinical research accomplishments provide a foundation for consulting with various groups including the U.S. EPA on its health research program and asthma strategy." A more comprehensive article has been included in the Council Agenda Book or will be available shortly on the EPA website (http://www.epa.gov/newsroom/)

STAFF HONORS and AWARDS

Kenneth Olden, Ph.D.; Director, National Institute of Environmental Health Sciences and *William A. Suk, Ph.D., MPH*; Director, Center for Risk and Integrated Sciences; Director, Superfund Basic Research Program, National Institute of Environmental Health Sciences were among six leaders in

Federal Agencies where recognized with a Commendation for their contributions to children, environmental health, and the special needs of oceanic peoples at the 21st International Neurotoxicology Conference: Infant and Child Neurotoxicity Studies, February 10-14, 2004, Honolulu, Hawaii.

STAFF ACTIVITIES

Ms. Beard, WETB, presented "NIEHS Lessons Learned from Advanced Training Technologies" at the American Industrial Hygiene Conference & Expo 2003 (AIHCE 2004) in Atlanta, Georgia on May 8-9.

Dr. Thompson, CRIS, has been invited to serve on the EPA's World Trade Center Health Panel. The purpose of this expert review panel is to obtain greater input on ongoing efforts to monitor health effects for workers and residents impacted by the collapse of the World Trade Center. This panel is convened and led by the EPA. The expert panel will help guide EPA's use of available exposure and health surveillance databases and registries. It will characterize any remaining exposures and risks, identify unmet public health needs, and recommend any steps to further minimize the risks associated with the aftermath of the World Trade Center attacks. For the complete press release and additional information please see http://www.epa.gov/wtc/panel.

Ms. Duke, GMB, was an invited speaker at the National Council of University Research Administrators Region 1 Spring conference held in Sturbridge, Massachusetts, May 5. She presented the NIH Grants Policy Update.

Mr. Hughes, WETB, presented at the DHHS Secretary's Council on Public Health Preparedness Meeting in Washington, DC on May 4.

Ms. Beth Anderson, CRIS, was invited to participate in EPA's 19th Annual Regional Annual Risk Assessors meeting held in Boston Massachusetts, May 3- 7. Ms. Anderson presented an overview of the Superfund Basic Research Program and highlighted recent Program advances.

Dr. Van Houten, PAB, was an invited speaker at the fourth International Workshop on DNA Repair, which was held in Smolenice, Slovokia, May 2-5. His lecture was "How do nucleotide excision repair proteins detect and remove DNA damage?" He also presented the final closing remarks to this meeting of 80 participants from more than 10 different countries.

Drs. Kirshner and Lawler, COSPB, organized and chaired a symposium "New Paradigms For Exploring Gene-Environment Behavior Relationships" on April 28 at the NIEHS Rodbell Auditorium, Research Triangle Park, North Carolina. The goal of the symposium was to identify and enhance research in the field of behavioral toxicology.

Dr. Van Houten, PAB, presented a lecture "DNA damage processing by the UVrABC nuclease system: probing the DNA hand-off using protein-DNA cross-linking agents" on April 23 at Vanderbilt Institute of Chemical Biology Mass Spectrometry Center, Nashville, Tennessee. Dr. Dan Liebler hosted the seminar.

Mr. Hughes, WETB, and staff sponsored a Technical Workshop on Training Partnerships for Prevention, Protection, and Preparedness. This workshop focused on building stronger relationships with the Department of Homeland Security (DHS), the Department of Labor (DOL/OSHA), and the Environmental Protection Agency (EPA/OSWER) for the training of responder populations most at risk, particularly fire fighters, health care workers, and the construction trades needed at disaster response. The workshop was held in Washington, DC on April 22-23. Other staff attending the workshop and participating in various activities included *Ms. Beard, Mr. Outwater, and Ms. Thompson, WETB.* On April 21, the semi-annual WETP Awardee Meeting was held. *Ms. Mason, GMB,* also participated in the meeting.

Dr. Van Houten, PAB, was a co-chair of a "Workshop on DNA Adducts: Biological Consequences and Application to Risk Assessment, " which was co-sponsored by the International Life Sciences Institute and

NIEHS. The meeting, attended by over 120 scientists from academia, government and private industry was held April 13-14 in Washington, D.C. The day and a half meeting considered the current knowledge of the chemistry and biology of DNA adducts and discussed the use of DNA adducts in developing a more mechanistic risk assessment on the consequences of DNA lesions.

Dr. Van Houten, PAB, gave an invited lecture, "How do proteins find DNA damage: Structure-function studies of nucleotide excision repair proteins," on April 7 at the Department of Chemistry, University of North Carolina, Chapel Hill, North Carolina. Dr. Dorothy Erie hosted his visit.

Mr. Hughes, WETB, presented at the 5th Biennial Freshwater Spills Symposium on April 6-8 in New Orleans, Louisiana, on a session concerning Emergency Response and Counter-Terrorism Issues.

Mr. Hughes, WETB, presented an update on the Worker Education and Training Program at the HAMMER Steering Committee Meeting in Washington, DC on April 2.

Drs. Packenham and Maull, SPHB, organized, managed, and hosted a Mid-Program Retreat entitled "Assessing and Refining Our Program," for the Comparative Mouse Genomics Centers (CMGC) Consortium, held at the National Institute of Environmental Health Sciences on March 26-27. The goal of this retreat was to discuss the past, present and future of the CMGCC. Discussions centered on accomplishments to date, including technical capabilities developed, organizational structure, and potential future directions for the Consortium. Participants included the CMGC Directors and Co-directors, NIEHS Extramural Staff (*Dr. Collman, SPHB, Ms. Winters and Ms. Garcia, GMB, and Dr. Leroy Worth, SRB*), NIEHS Computer Specialist (Mr. Nehls), members of the CMGC Consortium Mouse Task Force, and external reviewers.

Dr. Van Houten, PAB, gave a lecture, "Telomerase present in the mitochondria increases hydrogen peroxide-induced mitochondrial DNA damage" on March 24 at the Center of Excellence in Biomedical and Marine Biotechnology, Florida Atlantic University, Boca Raton, Florida. His hosts were Drs. Herb Weissbach and Zingwei Li.

Dr. Tyson, SPHB, gave an overview of extramural K-12 EHS science education programs and the COEP Resource Center at the NCABR Science Teachers Workshop on March 23 at NIEHS, Research Triangle Park, North Carolina.

Dr. Allen, SRB, was invited to serve as one of five panelists in a Grantsmanship Workshop held March 23, 2004 at Sigma Xi, Research Triangle Park, North Carolina. The workshop was co-sponsored by Sigma Xi (the Research Honor Society) and Office of Fellows' Career Development, Office of the Director, NIEHS/NIH. The panelists spoke about the importance of networking/collaborations (as they relate to writing applications) and the grant review process. Sixteen of the twenty-six participants were NIEHS fellows. This was a great opportunity to help mentor a young scientists from the NIEHS and the Research Triangle Park area.

Mr. O'Fallon, SPHB, worked with Maryland Public Television (MPT) and Johns Hopkins University (JHU) staff to organize the Environmental Health Sciences as an Integrative Context for Learning (EHSIC) grantee meeting in Baltimore, Maryland, March 21-22. The EHSIC grantee meeting was hosted by MPT and JHU in conjunction with the annual Society of Toxicology conference. Grantees focused on three primary themes: (1) strategic planning for publications and dissemination of their curricular materials to school systems, (2) using the media to communicate project activities and to disseminate research findings, and (3) Federal science education directions, policies and programs. *Dr. Anne Sassaman* presented on continued NIEHS commitment to science education. *Ms. Lou Rozier* (NIEHS/Office of Communication and Public Liaison) spoke on the importance of working with NIEHS on development of Press Releases for the dissemination of research findings.

Mr. O'Fallon, SPHB, collaborated with Dr. David Eaton of the University of Washington to organize and moderate a three-hour science education workshop at the Society of Toxicology conference on March 25 in Baltimore, Maryland. The workshop, "Novel approaches to engaging toxicologists in K-12 science education and outreach," highlighted many successful models of NIEHS grantees going into the K-12 classroom to increase awareness of, and enthusiasm for, science (in general) and environmental health (specifically). The workshop also included a hands-on session where meeting participants had the opportunity to interact with grantees and learn about new lessons or activities they can use in the classroom.

Dr. Shreffler, COSPB, presented a session on Training Opportunities for Students and Institutions and conducted a round table discussion with student mentors at the Undergraduate Education Program on March 21 at the Society of Toxicology Meeting in Baltimore, Maryland. The Undergraduate Education Program is conducted by the Education Committee of the SOT for minority students and their advisors to familiarize them with career opportunities in toxicology, and provide information on graduate schools and the application process.

Dr. Sassaman, OD, was a speaker at the Grantsmanship Forum at the annual meeting of the Society of Toxicology. The title of her presentation was "New Program Opportunities at NIEHS and How to Take Advantage of Them."

NIEHS hosted the current class of NIH Extramural Associates on March 16. *Dr. Ethel Jackson, OD*, coordinated the visit to NIEHS and EPA, and *Dr. Sassaman* presented the Institute's background and extramural programs. This is a program for faculty for minority and women's institutions to become familiar with opportunities for NIH funding and to serve as a resource at their home institutions for faculty research development.

Dr. Tyson, SPHB, was a speaker at the University of Miami Freshwater and Marine Biological Science Center's Research Symposium in Miami, Florida on March 18 and at the Florida International University's ARCH External Advisory Committee Meeting in Miami, Florida on March 19.

Mr. O'Fallon, SPHB, working actively with staff from across the NIEHS, led the development of a cross-institute science education website (http://www.niehs.nih.gov/science-education/). The new website targets three primary audiences: students, teachers, and scientists. The purpose of the site is to provide users with easy access to reliable tools, resources and classroom materials. The site was unveiled March 17 in time for Excellence in Science, Technology, and Mathematics Excellence week. This is the first version of the website. It will be updated to make it even easier to find environmental health materials that can be used in the classroom.

Dr. Heindel, COSPB, and Carol Henry, Ph.D. DABT, Vice President, Science and Research, American Chemistry Council (ACC) organized and co-chaired a meeting of the grantees funded from two NIEHS initiatives. Grantees from the Joint NIEHS/ACC funded Developmental Toxicology RFA and those funded in the first year of the Fetal Basis of Adult Disease program announcement presented their data on March 8-9 at the Marriott Hotel in Research Triangle Park, North Carolina. The goal of this meeting was to assess the success of the Developmental Toxicology RFA and to assess the progress of the grantees funded under the Fetal Basis initiative. In addition, the meeting served to introduce grantees from these separate initiatives in developmental toxicology to each other with the goal of stimulating cross fertilization and collaborations.

Ms. Duke, GMB, participated as a member in the planning committee for the Annual North Carolina Society of Research Administrators Conference held in Durham, North Carolina, March 2 - 4. She was an invited speaker at that conference, presenting a session entitled "NIH Grant Initiatives and Policy Update" which focused on the NIH Roadmap activities as well as new NIH grants policy updates. She also facilitated a roundtable discussion on "Terms and Conditions of NIH Grant Awards."

Dr. Srinivasan, SPHB, served on the National Commission on Community-Engaged Scholarship in the Health Professions to take a leadership role in creating a more supportive culture and reward system for health professional faculty involved in community-based participatory research, service-learning and other forms of "community-engaged scholarship." This Commission was convened by the Community-Campus Partnerships for Health. The Commission met in March 2004 in Washington, DC.

Drs. Heindel, Mastin and Shreffler,COSPB, presented a grantsmanship workshop for postdoctoral fellows in the NIEHS Intramural Program on March 2. This forum was designed to aid interested IRTA fellows in the preparation of their application to the Transition to Independent Position Grant Program.

Drs. Reinlib, Maull, and Collman, SPHB, in collaboration with NCI, organized and coordinated, the second planning meeting of the Breast Cancer and the Environment Research Centers Network February 25-26, in Georgetown, Washington, D.C. All official (Biology, Epidemiology, and COTC) and ad hoc (Bioinformatics and Scientific Meeting Planning) subcommittees met and provided updates at the Steering Committee meeting, held on February 26. BC/E Working Group representatives were present at all subcommittee meetings and at the Steering Committee meeting. Ms. Fran Visco, President, National Breast Cancer Coalition, provided remarks to the participants at a working lunch.

Ms. *Beard, WETB*, participated in the development and evaluation of the OSHA/NIEHS Disaster Site Worker Response Training on February 29 in Washington, DC.

Dr. Balshaw, CRIS, organized a meeting of the grantees under the NIEHS Functional Proteomics Initiative May 3-4. The meeting included an afternoon symposium with invited speakers.

UPCOMING MEETINGS and WORKSHOPS

The Office of the Director, NIEHS, is organizing the "Obesity and Built Environment Conference" to be held at the Marriott Wardman Park, Washington DC, May 24-26. *Dr. Srinivasan, SPHB,* is on the Planning Committee for the conference.

Mr. Outwater, WETB, along with *Dr. Mastin, COSPB*, will participate in the NIEHS co-sponsored national conference entitled "Mold-Related Health Effects: Clinical, Remediation Worker Protection, and Biomedical Research Issues on June 28-29. The purpose of the cross-disciplinary meeting is to bring together experts in clinical science, worker protection and education, and basic research to further efforts to prevent, diagnose, and treat conditions related to exposure to indoor mold.

The third annual Comparative Mouse Genomics Centers (CMGC) Consortium Summer Symposium, "Cell Cycle and DNA Repair Variants" will be hosted by The University of Texas M.D. Anderson Cancer Center CMGC, June 1 – 3, in Austin, Texas. The focus of the symposium will be on recent findings concerning the function of DNA repair and cell cycle control genes and how these functions are altered by naturally occurring polymorphisms in the human population. The symposium will highlight the use of molecular epidemiological studies, in vitro assays, and mouse modeling to identify and functionally characterize polymorphisms relevant for environment-related diseases. For additional information please see the meeting website: http://sciencepark.mdanderson.org/cmgcc/symposium/ *Drs. Packenham, Maull, and Collman, SPHB*, will attend.

Dr. Packenham, SPHB, will co-chair a one-day satellite meeting, *Phenotyping Forum*, June 3 – 4, also in Austin, Texas. This forum is a coordinated effort with the NIEHS CMGC Consortium, the NCI Mouse Models for Human Cancer Consortium and the NCRR Mutant Mouse Regional Resource Consortium to initiate discussions and begin development of Phenomics protocols for mouse phenotyping. The meeting will bring together a small group of Nationally and Internationally renowned scientists with expertise in mouse pathology to explore new methodologies for mouse phenotyping. *Dr. Maull, SPHB*, will participate in this meeting.

The Superfund Basic Research Program is co-sponsoring a PCB Workshop in Champaign/Urbana, Illinois, June 13-15. This workshop will bring together scientists who are concerned with the physical and chemical as well as the biomedical aspects of the detection, movement, metabolism, toxicity, remediation and risk assessment of PCBs. A primary objective is to encourage interactions and the exchange of information and to compose a new, up-to-date compendium on the very latest findings relating to the chemistry and biology of PCBs and their risk to human health. Other sponsors include the University of Kentucky Superfund Basic Research Program, the Environmental Protection Agency, the Hanson-Drucker Heritage Fund, and the University of Iowa's Environmental Health Sciences Center and Fogarty International Center.

Dr. Maull, SPHB, will participate in the Botanical Research Centers Annual Directors' Meeting, planned for August 5 through 7, 2004. This year's meeting is being hosted by the University of Missouri/Columbia Botanical Center, Dennis Lubahn, Center Director. The Botanical Research Centers Program is a joint program between NIEHS, the Office of Dietary Supplements, and the National Center for Complementary and Alternative Medicine.

Dr. Suk, CRIS, has accepted an invitation to be a member of the International Advisory Board for the upcoming "5th Princess Chulabhorn International Science Congress: Evolving Genetics and Its Impact on the World," to be held August 16-20, 2004, Bangkok, Thailand. He also has been asked to give a plenary lecture on translating genomics to reduce risk of exposure and disease, and he is involved in organizing as symposium on gene-environment interaction.

A meeting on Brownfields 2004: Growing a Greener America Conference in St. Louis, Missouri on September 20. *Ms. Beard and Mr. Outwater, WETB*, are planning to conduct a grantee meeting of the Brownfields Minority Worker Training Program in conjunction with this meeting.

The NIEHS Basic Research Program, in conjunction with the Mt. Sinai Superfund Basic Research Program and the Hudson River Foundation, is sponsoring a conference on "Persistent Contaminants: New Priorities, New Concerns" in Bear Mountain, New York, September 29-30. The intent of this conference is to examine the environmental distribution and potential human health risks of persistent contaminants with a focus on two members of a new and increasingly widespread generation of environmental pollutants -- the alkylphenol ethoxylates (APEs) and the polybrominated diphenylethers (PBDEs).

The NIEHS Superfund Basic Research Program, in conjunction with the Agency for Toxic Substances and Disease Registry and the Texas A&M University School of Rural Health, is sponsoring the "Central and Eastern European Environmental Health Conference: International Health Sciences Solving Common Problems," to be held in Prague, Czech Republic, October 24- 27. The Central and Eastern European Environmental Health Conference has three primary objectives: (1) to gather scientists and students from the US and Central and Eastern Europe to discuss the magnitude of the problem in understanding the health effects that could result from exposure to hazardous substances, specifically in regions of Central and Eastern Europe; (2) to discuss improved methods for assessing exposure including biomarkers of exposure and integrated methods for predicting dose; and (3) to discuss specific health effects associated with exposure to chemicals at these sites with a focus on developmental and reproductive health.

STAFF CHANGES

Recruitments

Teresa (Terry) Nesbitt, D.V.M, Ph.D., has accepted the position of Chief, Scientific Review Branch effective May 30. She spent 17 years at Duke before going to NIH/CSR in 1998 to be Scientific Review Administrator for the Surgery and Bioengineering Study Section. She has been chief of review at NIAMS since last year. A more detailed report will be provided for September Council.

Sally Tinkle, Ph.D., has accepted the position of Program Administrator for the Respiratory Diseases Program effective June 13. A more detailed report will be provided for September Council.

Ms. Margarita Roque has accepted the lead Administrative Officer position, which will take effect upon the retirement of Mr. Warren Pope. Ms. Roque is currently the second Administrative Officer in DERT.

Ms. Anne Thompson has been selected for a Program Analyst position in the Program Analysis Branch.

Departures:
Mr. Warren Pope, Administrative Officer for DERT, has announced his retirement, effective June 3, 2004.